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Palliative Cancer Care Guidelines

Updated: Jun 01, 2019 | Author: Winston W Tan, MD, FACP; more...

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Palliative Care Standards

The World Health Organization (WHO) describes palliative care as services designed to prevent and relieve suffering for patients and families facing life-threatening illness, through early management of pain and other physical, psychosocial, and spiritual problems. [1] There is growing recognition of palliative care as an integral aspect of cancer treatment, with the ability to improve quality of life and prevent unnecessary hospital admissions and the use of health services, especially when instituted early in the course of disease.

For example, Temel et al reported that in patients with metastatic non–small cell lung cancer, early palliative care led to significant improvements in both quality of life and mood. In addition, patients who received early palliative care had less aggressive care at the end of life and had longer survival than patients who received standard oncologic care alone. [2] Findings such as those have prompted the development of a range of guidelines concerning palliative cancer care. [1, 3]

The American Society for Clinical Oncology (ASCO) recommends considering the combination of palliative care with standard oncology care early in the course of treatment for patients with metastatic cancer and/or a high symptom burden. [4] Specific recommendations are as follows:

- The time to start palliative care is as soon as a patient's cancer becomes advanced
- For newly diagnosed patients with advanced cancer, the Expert Panel suggests early palliative care involvement within 8 weeks after diagnosis
- Inpatients and outpatients with advanced cancer should receive dedicated palliative care services early in the disease course concurrent with active treatment.

According to ASCO, essential components of palliative care may include the following [4] :

- Building rapport and relationships with patients and family caregivers
- Managing symptoms, distress, and functional status (eg, pain, dyspnea, fatigue, sleep disturbance, mood, nausea, constipation)
- Exploration of understanding and education about illness and prognosis
- Clarification of treatment goals
- Assessment and support of coping needs (eg, provision of dignity therapy)
- Assistance with medical decision making
- Coordination with other care providers
- Provision of referrals to other care providers as indicated

ASCO recommendations on delivery of palliative care are as follows [4]

- For patients with cancer who have high symptom burden and/or unmet physical or psychosocial needs, outpatient cancer care programs should provide and use dedicated resources (palliative care clinicians) to deliver palliative care services to complement existing program tools.
- For patients with early or advanced cancer who will be receiving care from family caregivers in the outpatient setting, providers (eg, nurses, social workers) may initiate caregiver-tailored palliative care support, which could include telephone coaching, education, referrals, and face-to-face meetings.
- Telephone support may be offered for family caregivers who may live in rural areas or are unable to travel to the clinic.

The National Comprehensive Cancer Network (NCCN) concurs and includes the following additional recommendations [5] :

- All cancer patients should be repeatedly screened for palliative care needs, beginning with their initial diagnosis and thereafter at intervals as clinically indicated
- Palliative care should be initiated by the primary oncology team and then augmented by collaboration with palliative care experts
- All health care professionals should receive education and training to develop palliative care knowledge, skills, and attitudes
- An interdisciplinary team of palliative care specialists should be available to provide consultation or direct care to patients and/or families as requested or needed
- Quality of palliative care should be monitored by institutional quality improvement programs

The NCCN recommends assessment by the oncology team for patients whose screening confirms the presence of one or more of the following [5] :

- Uncontrolled symptoms
- Moderate-to-severe distress related to cancer diagnosis and cancer therapy
- Serious comorbid physical, psychiatric, and psychosocial conditions
- Patient, family, or caregiver concerns about the course of disease and decision-making
- Patient/family requests for palliative care
- Metastatic solid tumors and refractory hematologic malignancies
- Potentially life-limiting disease

Additional indicators may include the following:

- Poor performance status – Eastern Cooperative Oncology Group (ECOG) score ≥3 or Karnofsky Performance Status (KPS) score ≤50
- Persistent hypercalcemia
- Brain or cerebrospinal fluid metastasis
- Delirium
- Malignant bowel obstruction
- Superior vena cava syndrome
- Spinal cord compression
- Cachexia
- Malignant effusions
- Palliative stenting or venting gastrostomy

Cancer Pain

Optimal pain control is essential for the cancer patient. This can be achieved through local treatment with radiation, injections, or surgery, or systemic treatment with the appropriate analgesics. Early referral to a pain specialist who understands the needs of the patient is important. Pain should be considered a vital sign to assess at every visit of a cancer patient.

National Comprehensive Cancer Network (NCCN) guidelines identify general principles of pain management and provide specific recommendations for assessment, management, and reassessment of cancer pain in adults. Major recommendations include the following [6] :

- Consider interventions in the context of patient-specific goals for comfort, function, and safety
- Patients with an acute pain crisis may be candidates for hospital admission to achieve goals for comfort and function
- Identify pain related to an oncologic emergency
- For pain not related to an oncologic emergency, discriminate opioid-tolerant patients from opioid-naïve patients (ie, those with versus those without long-term exposure to opioids)

Assessment

Assessment recommendations are as follows:

- All patients should be screened for pain at every contact
- Pain intensity must be quantified and documented and the quality characterized by the patient, whenever possible
- Include patient reporting of breakthrough pain, treatments used and their impact on pain; patient reporting of adequate comfort; patient reporting of satisfaction with pain relief; provider assessment of impact on function; and any special issues for the patient relevant to pain treatment
- Comprehensive pain assessment for persisting pain or new pain should be performed to determine the etiology, pathophysiology, specific cancer pain syndrome, and patient goals for comfort and function

Management

Cancer pain management guidelines from the European Society for Medical Oncology (ESMO) follow the WHO strategy of a sequential three-step analgesic ladder from non-opioids to weak opioids to strong opioids, gauged to pain intensity. [7] ESMO recommendations for choice of analgesics according to pain severity are as follows:

- Mild – Acetaminophen (paracetamol) and/or a nonsteroidal anti-inflammatory drug (NSAID); those agents are also effective as adjuncts for treating more severe pain, at least in the short term and unless contraindicated
- Mild to moderate – Weak opioids such as codeine, tramadol, and dihydrocodeine, in combination with non-opioid analgesics
- Moderate to severe - Oral morphine

ESMO guidelines note that although oral administration is advocated, patients presenting with severe pain that needs urgent relief should be treated and titrated with parenteral opioids, usually subcutaneous or intravenous. [7]

ESMO recommendations regarding alternative strong opioids include the following:

- Oral hydromorphone or oxycodone (immediate-release and modified-release) and oral methadone are effective alternatives to oral morphine; however, methadone should be initiated by physicians with experience and expertise in its use
- Transdermal fentanyl and transdermal buprenorphine are best reserved for patients whose opioid requirements are stable, and are usually the treatment of choice for patients who are unable to swallow, have poor tolerance of morphine, r poor compliance
- Buprenorphine has a role in the analgesic therapy of patients with renal impairment and undergoing hemodialysis treatment
- Opioid switching to improve pain relief and/or drug tolerability is not supported by high-quality evidence but is frequently used in clinical practice; it requires requires familiarity with equianalgesic doses of the different opioids

For pain related to an oncologic emergency, such as bone fracture, infection, or obstruction, the NCCN recommends treating the pain directly in addition to providing specific treatment for the underlying condition (eg, surgery, steroids, radiation therapy, antibiotics). For pain not related to an oncologic emergency, NCCN recommendations vary according to whether the patient is opioid naïve or opioid tolerant. The U.S. Food and Drug Administration (FDA) defines opioid tolerance as receiving, for 1 week or longer, one of the following [8] :

- 60 mg oral morphine/day
- 25 mcg transdermal fentanyl/hour
- 30 mg oral oxycodone/day
- 8 mg oral hydromorphone/day
- 25 mg oral oxymorphone/day
- An equianalgesic dose of another opioid

For opioid-naïve patients, the NCCN recommends the following non–oncologic emergency pain management [6] :

- Provide psychosocial support, including education of the patient and family
- Reevaluate at each contact
- Consider adjuvant analgesics for specific pain syndromes
- Optimize integrative interventions
- Provide a prophylactic bowel regimen for patients receiving opioid analgesics
- Severe pain: For acute, severe pain or pain crisis, consider hospital or inpatient hospice admission to achieve patient-specific goals for comfort and function
- Moderate pain: Non-opioids and adjuvant therapies as appropriate (eg, acetaminophen, nonsteroidal anti-inflammatory drugs, antidepressants, anticonvulsants), with short-acting opioids as needed; if the patient consistently requires 3-4 doses daily, consider the addition of long-acting opioid; for persistent pain, initiate a regular schedule of opioid with rescue dose as needed
- Mild pain: First consider non-opioids and adjuvant therapies, unless these are contraindicated due to adverse effects or potential drug interactions

For opioid-tolerant patients who have breakthrough pain of intensity ≥4 (on a scale of 0-10) or whose goals of pain control and function are not met, management is as follows [6] :

- Administer a rescue dose of a short-acting opioid, equivalent to 10-20% of the total long-acting or regularly schedule oral opioid dose taken in the previous 24 hours
- Assess efficacy and adverse effects every 60 minutes for oral opioids and every 15 minutes for IV opioids
- If pain assessment is unchanged or increased, increase the rescue dose by 50-100%
- If the pain score decreases, repeat the opioid dose and reassess at 60 minutes for oral opioids and 15 minutes for IV opioids
- If the pain score remains unchanged after two to three cycles, consider changing the route of administration from oral to IV or explore alternative management strategies
- If the pain score decreases to 0-3, give the current effective dose as needed over 24 hours before proceeding to subsequent management strategies
- Ongoing need for repeated rescue doses may indicate a need for adjustment of the regularly scheduled opioid dose
- Consider rapidly acting transmucosal fentanyl for brief episodes of incident pain not attributed to inadequate dosing of around-the-clock opioid

Subsequent management is based on the continued pain rating score and includes the following:

- Regular doses of opioids, with rescue doses as needed
- Management of constipation
- Social support and education for patients and families

For ongoing care, if an acceptable level of comfort and function has been achieved and the patient's 24-hour opioid requirement is stable, convert to an extended-release oral medication (if feasible) or other extended-release formulation (e, transdermal fentanyl).

In 2012 the European Association for Palliative Care (EAPC) updated its guidelines for the use of opioid analgesics to treat cancer pain and provided the following recommendations [9] :

- For mild to moderate pain not controlled by NSAIDs, a step II oral opioid (codeine or tramadol) may be added; a step III opioid (eg, morphine or oxycodone) may also be considered
- There is no preference among oral morphine, oxycodone, or hydromorphone as first-choice step III opioids for moderate to severe pain
- Transdermal fentanyl and buprenorphine are alternatives to oral opioids for patients unable to swallow
- Patients experiencing inadequate relief and severe adverse effects with a step III opioid may benefit from switching to an alternative opioid
- Subcutaneous delivery is the preferred alternative for patients unable to receive opioids orally or transdermally; IV infusion should be considered when subcutaneous administration is contraindicated; IV infusion is preferred for opioid titration when rapid pain control is needed

Dyspnea

Management of dyspnea includes treatment of the physical and emotional needs of the patient.

The NCCN guidelines for treatment of dyspnea in cancer patients are based on estimates of the patient's life expectancy. [5] For patients with a life expectancy of years to months to weeks, the NCCN recommends assessment of symptom intensity followed by treatment of underlying causes or comorbid conditions with measures such as the following:

- Chemotherapy and/or radiation therapy
- Procedure to reduce or remove cardiac, pleural or abdominal fluid
- Bronchoscopic therapy
- Bronchodilators, diuretics, steroids, antibiotics, or transfusions
- Anticoagulants for pulmonary emboli

For symptomatic relief, the following interventions may be used, as appropriate:

- Oxygen therapy for hypoxia
- Educational, psychosocial, and emotional support for patients and family
- Nonpharmacologic therapies including fans, cooler temperatures, stress management, relaxation therapy, and comfort measures
- If the patient is opioid naïve, morphine; if dyspnea is not relieved by morphine and is associated with anxiety, add benzodiazepines
- Noninvasive positive-pressure ventilation (ie, continuous positive airway pressure [CPAP], biphasic positive airway pressure [BiPAP]) if clinically indicated for a severe reversible condition

For patients with a life expectancy of weeks to days, the following measures may be used, in addition to the interventions listed above:

- When assessing symptom intensity, use physical signs of distress as potential indications of dyspnea in noncommunicative patients
- Withhold, withdraw, or initiate a time-limited trial of mechanical ventilation as indicated by patient and family preferences, prognosis, and reversibility
- Provide sedation as needed
- Provide guidance for patient and family regarding dying and respiratory failure
- Provide emotional and spiritual support

If fluid overload is a contributing factor, interventions include the following:

- Decrease/discontinue enteral or parenteral fluid
- Consider low-dose diuretics
- If opioid naïve, morphine
- Benzodiazepines
- Scopolamine to reduce excessive secretions

The only treatment for dyspnea recommended in the Oncology Nursing Society (ONS) guidelines is parenteral or oral immediate-release opioids. For patients with a life expectancy of years to months to weeks, the ONS deemed the following interventions "likely to be effective" [10] :

- Temporary ventilator support for severe, reversible conditions
- Oxygen therapy
- Benzodiazepines for anxiety
- Increasing ambient airflow directed at the face or nose
- Providing cooler temperatures
- Promoting relaxation and stress reduction
- Providing educational, emotional, and psychosocial support for patients and family caregivers, and referring to other disciplines as appropriate

For patients with a life expectancy of weeks to days, the ONS recommendations are as follows:

- Reduce excessive secretions with scopolamine, hyoscyamine, or atropine
- Implement oxygen therapy, if the patient reports subjective relief with it
- Institute sedation as needed
- Discontinue fluid support; consider low-dose diuretics if fluid overload may be a contributing factor

Anorexia/Cachexia

Guidelines for the management of anorexia/cachexia in patients with advanced cancer have been issued by the NCCN and the European Palliative Care Research Collaborative (EPCRC).

The NCCN guidelines are based on estimates of the patient's life expectancy. [5] For patients with a life expectancy of years to months, the recommendations are as follows:

- Evaluate the severity of weight loss
- Treat reversible causes – Early satiety; symptoms that interfere with food intake (eg, depression, pain, constipation, nausea/vomiting, fatigue, dyspnea)
- Modify medications that interfere with intake
- Consider possible endocrine disorders – Hypogonadism, thyroid dysfunction, metabolic abnormalities (eg, increased calcium)
- Consider appetite stimulant – Megestrol acetate (should be used with caution due to increased risk of blood clots, edema; death occurs in one of every 23 patients, prednisone
- Consider exercise program
- Consider consultation with a nutritionist
- Consider enteral and parenteral feeding as appropriate

For patients with a life expectancy of months to weeks to days, the NCCN recommends first determining the importance of the symptoms to patient and family; if considered important, the anorexia/cachexia can be treated with megestrol acetate. Further recommendations are as follows:

- Focus should be on patient goals and preferences
- Provide emotional support
- Treat depression, if appropriate
- Provide education and support to patient and family regarding the emotional aspects of withdrawal of nutritional support

Finally, inform the patient and family of the natural history of advanced cancer, including the following:

- Absence of hunger and thirst is normal
- Nutritional support may not be metabolized
- There are risks associated with artificial nutrition and hydration, including fluid overload, infection, and hastened death
- Symptoms such as dry mouth can be treated with local measures (eg, mouth care, small amounts of liquids)
- Withholding or withdrawal of enteral or parenteral nutrition is ethically permissible; it will not exacerbate symptoms and may improve some symptoms

The EPCRC guidelines focus on refractory cachexia in patients with advanced cancer, which it defines as "a stage where reversal of weight loss is no longer possible due to very advanced or rapidly progressive cancer unresponsive to anti-cancer therapy." The recommendations in the guidelines are aimed at alleviating the consequences and complications of cachexia and eating-related distress of patients and families and include the following [11] :

- Educate patient and family to minimize eating-related distress; counsel them about weight loss–related distress and end-of-life issues
- Enteral nutrition therapy may be partially effective for selected patient groups
- The burden of parenteral nutrition will outweigh any benefits in the majority of patients
- The use of thalidomide is not recommended
- The use of cannabinoids is not recommended
- Progestins should be considered for patients with anorexia as a major distressing symptom
- Steroids may be given for short periods (at most 2 weeks); longer duration may increase the burden on the patient from side effects and may cause a deterioration in muscle strength

Distress Management

The NCCN guidelines for distress management include recommendations for ongoing screening, monitoring, documentation, and treatment of distress throughout all stages of cancer treatment. [12] Screening for distress using the Distress Thermometer and Problem Checklist should be conducted at the initial visit and at other appropriate intervals, especially with changes in disease status (ie, remission, recurrence, or disease progression).

Treatment is determined on the basis of the level and source(s) of distress identified. Clear roles are delineated for members of the primary oncology team as well as for psychosocial oncology professionals who deliver mental health services, social work and counseling services, and chaplaincy services. [7]

In 2014, ASCO released evidence-based guidelines for managing depression and anxiety in patients with cancer. [13] These guidelines were adapted from the 2010 Pan-Canadian Practice Guideline: Screening, Assessment and Care of Psychosocial Distress (Depression, Anxiety) in Adults with Cancer, which was developed as a synthesis of five practice guidelines, including the NCCN guidelines for stress management. [14]

The ASCO guidelines identify separate processes for screening, assessment, and treatment of depression and anxiety in adults with cancer. Timing of evaluation, types of assessment tools, and specific treatment pathways are recommended depending on the levels of symptoms reported. Recommendations for follow-up and ongoing re-assessment are also provided. [13]

Appropriate referral to a psychologist and/or a psychiatrist is essential for the total care of the patient.

Palliative Sedation

In 2009, the European Association of Palliative Care (EAPC) published guidelines to address the key clinical issues surrounding palliative sedation. The recommendations in the guidelines are intended to be modified to reflect local culture; legal considerations; and specific needs of the home, hospital, or hospice-based setting. The recommendations include the following [15] :

- Sedation can be considered for patients with intolerable distress due to physical symptoms and a lack of other methods of palliation
- Continuous deep sedation should be considered only in the very terminal stages of illness with expected death within hours to days at most
- Evaluation should be performed by a clinician with expertise in palliative care; whenever possible, evaluation should be multidisciplinary
- Assessment should include estimates at to whether death is anticipated within minutes to hours, hours to days, days to weeks, or longer, and evaluation of the patient's capacity to make decisions about ongoing care; if decisional capacity is in doubt, evaluation by a psychiatrist may be required
- For patients with decisional capacity, the aims, benefits, and risks of the proposed sedation should be discussed with the patient and preferably with participation of family members
- For patients lacking capacity to decide, and without advance directives, permission should be obtained from a legally recognized proxy
- In actively dying patients who have no advanced directive or health care proxy and are in severe distress, comfort measures, including the use of sedation if necessary, is the standard of care
- If the family members are not participants in the decision process, permission should be sought to inform them of the decision
- The level of sedation should be the lowest level necessary to provide relief of suffering
- Intermittent or mild sedation should be attempted first

The presence of refractory psychological symptoms does not necessarily indicate a far advanced state of physiological deterioration; sedation should be reserved for patients in advanced stages of terminal disease under the following circumstances:

- Symptoms should be designated as refractory only after repeated assessment by clinicians with psychological treatment expertise who have established a relationship with the patient and family and have attempted routine approaches for anxiety, depression, and existential distress
- Evaluation should be conducted by a multidisciplinary team that includes psychiatrists, chaplains, ethicists, and persons providing direct care for the patient
- In the rare cases where sedation is appropriate, sedation should be delivered on a respite basis for 6-24 hours with planned downward titration
- Continuous sedation should be considered only after repeated trials of respite sedation with intensive intermittent therapy

The 2014 European Society of Medical Oncology (ESMO) guidelines for use of palliative sedation in advanced-stage cancer are derived from the EAPC guidelines and contain no major variances in the recommendations. [16]

NCCN guidelines for palliative sedation are also in general agreement with EAPC. Additional specific recommendations include the following [3] :

- Palliative sedation is best performed by palliative care experts
- The patient must have refractory symptoms that cannot be controlled despite aggressive palliative care that does not compromise consciousness, and death is anticipated within hours to days as confirmed by two physicians
- Reassignment of health care providers who cannot provide sedation due to personal or professional beliefs as long as patient care can safely be transferred to another health care professional
- Maintain current pain and symptom management interventions
- Monitor patient symptoms and titrate sedatives and other medications to maintain a level of sedation that relieves the patient's refractory symptoms
- Provide ongoing psychosocial and spiritual support for the patient's family and health care providers

Questions & Answers

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How does the WHO define palliative care?

What are the ASCO guidelines for the integration of palliative care into standard oncology care?

According to ASCO guidelines, what are the essential components of palliative cancer care?

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What are the NCCN guidelines for delivery of palliative care?

What are NCCN guidelines for palliative cancer pain management in opioid-naïve patients?

What are the NCCN guidelines on palliative care for cancer pain?

What are ESMO guidelines for palliative cancer pain management?

What is the FDA definition of opioid tolerance in palliative cancer care?

What are NCCN guidelines for palliative cancer pain management in opioid-tolerant patients?

What are the EAPC guidelines for palliative cancer pain management?

What are the NCCN treatment guidelines for dyspnea in palliative cancer care?

What are the ONS treatment guidelines for dyspnea in palliative cancer care?

What are the NCCN palliative cancer care treatment guidelines for cancer patients with anorexia/cachexia?

What are the EPCRC palliative care treatment guidelines for anorexia/cachexia?

What are the NCCN palliative cancer care guidelines for distress management?

What are the EAPC guidelines for palliative sedation in patients with cancer?

What are the NCCN guidelines for palliative sedation in patients with cancer?

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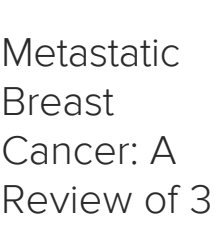

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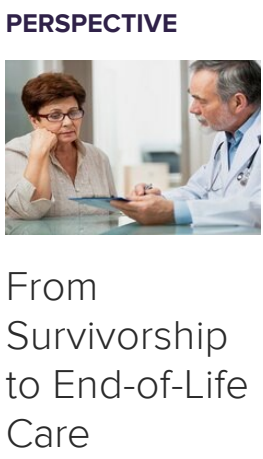

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